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(54) Title: TREATMENT WITH CYTOKINES

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(57) Abstract: An inflammatory process is suggested to be involved in the pathogenesis of Alzheimer's disease (AD), a neurodegenerative disorder characterized by the presence of neuritic plaques within the cerebral cortex that are mainly composed of a small insoluble protein of 40-42 aminoacids (amyloid protein). The biological correlates of this process are nevertheless not clear. Interleukin-10 (IL-10) is a cytokine that suppresses T lymphocytes and cell-mediated immunity in humans and mice and has potent anti-inflammatory properties. To verify if IL-10 production would be impaired in AD patients we stimulated PBMC of 47 patients and 25 age-matched healthy controls (HC) with a mitogen, a recall antigen or with amyloid peptides. IL-2 production was measured as well in the same cultural conditions. Results showed that amyloid-specific IL-10 generation is selectively and significantly reduced in AD patients (p= 0.023). Analyses on the alleles of the IL-10 gene revealed that the genotype associated with high IL-10 production is extremely infrequent in AD individuals (2% vs. 28%). The presence of low/intermediate IL-10-producing genotypes (GCC/ATA; ATA/ATA) was associated with an earlier age at disease onset and (ACC/ACC; ACC/ATA) with an accelerated rate of disease progression. These data shed light on the biology of the inflammatory process involved in the pathogenesis of AD by showing that the presence of low-IL-10-allelic isoforms results in an amyloid-specific impairment of IL-10 production and is associated with the clinical severity of AD. These results lend support to the use of anti-inflammatory compounds in the therapy of this disease.